

Extended Letrozole Regimen for Enhancing Follicular Response in PCOS-related Infertility

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Introduction

- PCOS is a major cause of anovulatory infertility.
- Letrozole is now the first-line agent for ovulation induction due to its superior efficacy and safety profile.¹
- While the standard regimen (2.5 mg for 5 days) is effective, extended regimens may enhance ovulatory response especially in resistant cases.

Objective

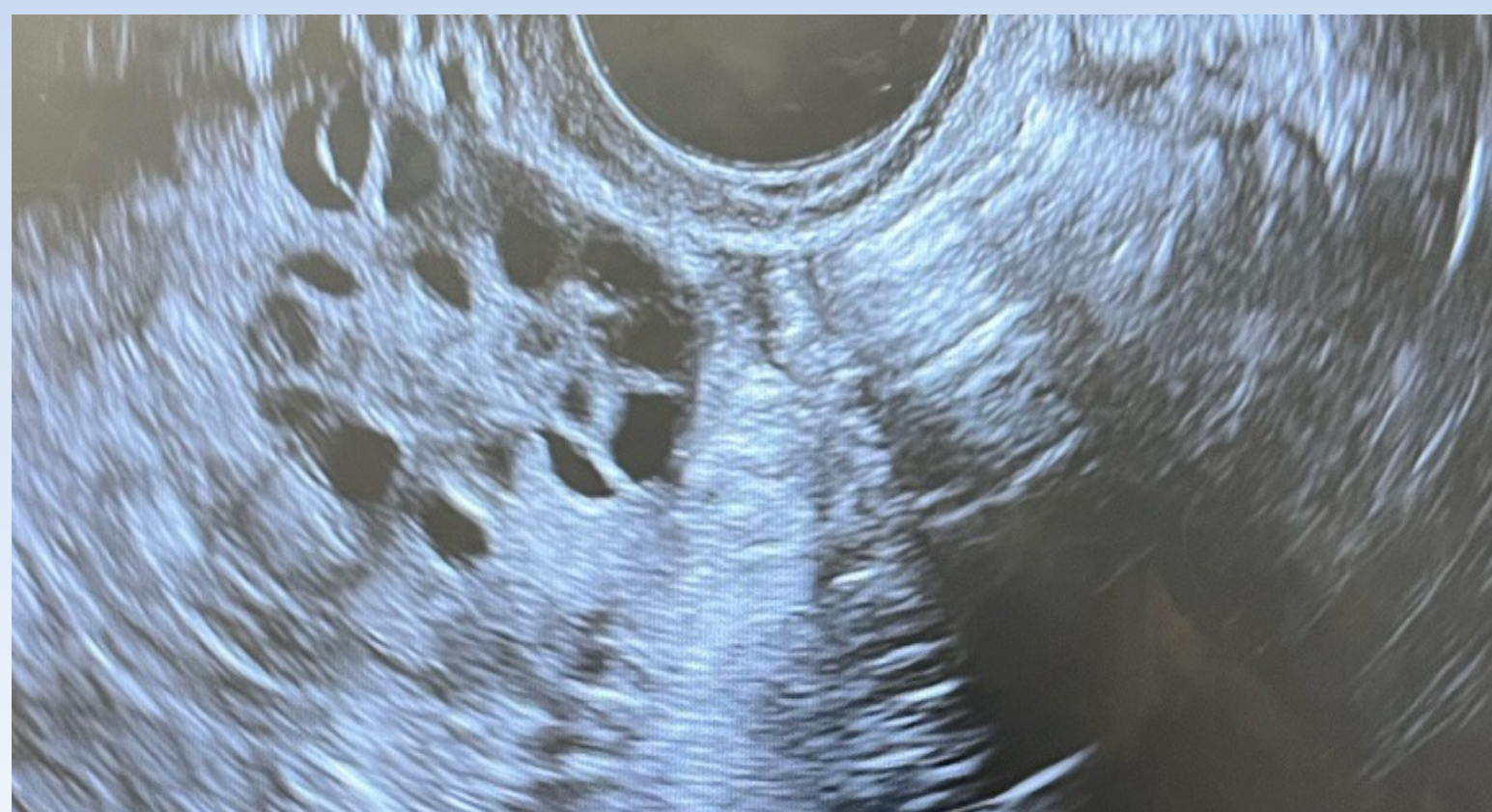
PRIMARY OBJECTIVE:

To compare the efficacy of a 10-day versus 5-day letrozole regimen in improving follicular response and pregnancy outcomes in women with PCOS-related infertility.

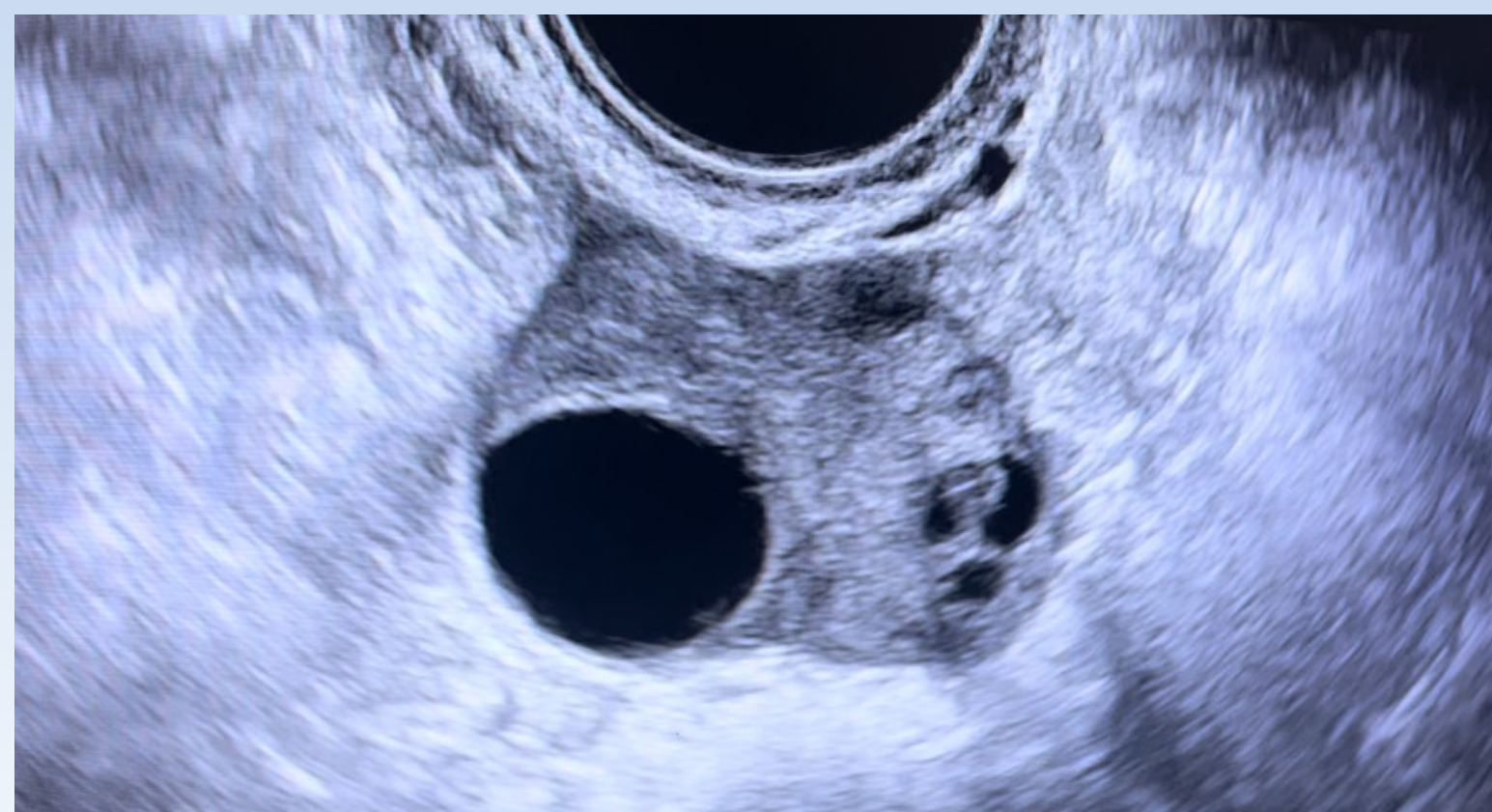
- SECONDARY OBJECTIVES:** Need for dose escalation
- Need for injection gonadotropin
- Multi-follicular development
- Ovarian hyperstimulation syndrome (OHSS) rate
- Clinical pregnancy rate and pregnancy rate per cycle
- Multiple pregnancy rate and abortion rate

Methods

- Prospective randomized controlled trial, conducted at a tertiary care center in North India.
- Between October 2023 to November 2024



D2 TVUS showing ovary with multiple small antral follicles



D14 TVUS showing dominant follicle

Consort diagram

100 Infertile women with PCOS undergoing ovulation induction treatment in the Department of Obstetrics and Gynaecology, AIIMS, New Delhi

Inclusion criteria:

- 21-38 years age
- Normal husband semen parameters
- At least 1 tube patent
- Controlled thyroid disorders/normal prolactin levels/ no ovarian surgery
- Not on any hormonal contraception or insulin sensitizers

Exclusion criteria:

- Age <20 years, >38 years
- H/o endometriosis
- Diminished ovarian reserve
- On any hormonal contraception or insulin sensitizers
- Uncontrolled thyroid disorder
- Hyperprolactinemia
- Non-classical congenital adrenal hyperplasia

Block randomization into 2 groups of N=80

Group A (Extended regimen N=40)
Tablet Letrozole 2.5 mg/day for 10 days on cycle days 2-11

Group B (Standard regimen N=40)
Tablet Letrozole 2.5 mg/day for 5 days on cycle days 2-6

D9 TVS-Follicular monitoring

Response

3 OI cycles/conception

Analysis N=40

Non-Response

Dose/drug upgradation

Analysis N=40

Discussion

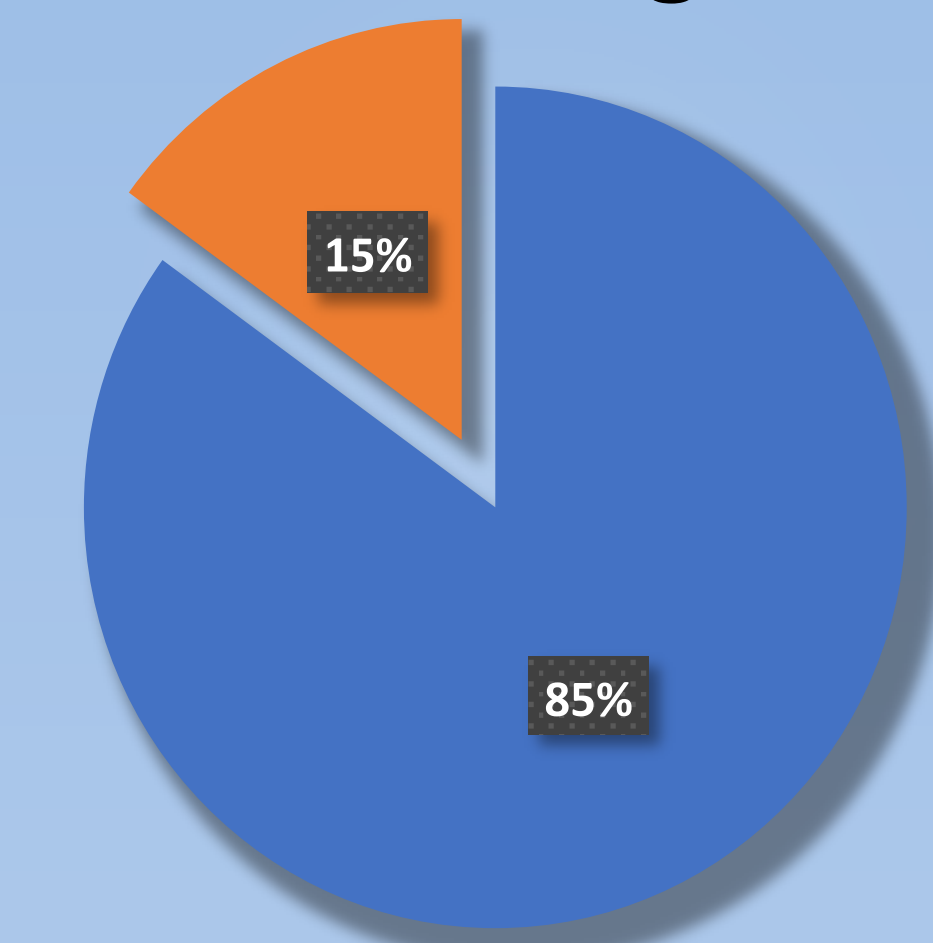
- Extended letrozole regimen (2.5 mg for 10 days) led to significantly higher follicular response (85% vs 52.5%, $p = 0.002$).
- Zhu et al. (2022) and Mandelbaum et al. (2024) all reported improved ovulation outcomes with extended letrozole regimens, supporting our findings.^{2,3}
- The extended regimen demonstrated a higher pregnancy rate per cycle (22.58% vs. 15.29%), indicating a potential for improved conception efficiency, although the difference was not statistically significant.

Results

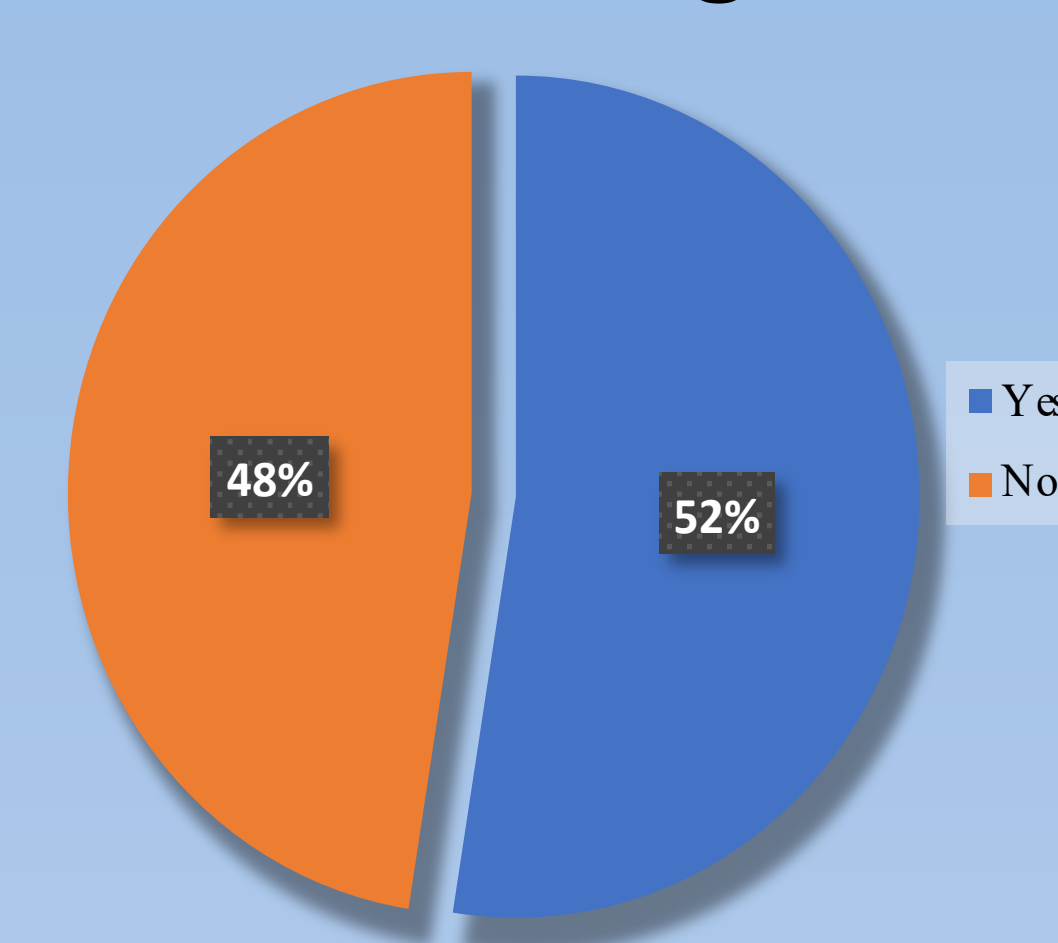
Primary Outcome: Follicular Response

Parameter	Regimen		
	Extended regimen (N=40)	Standard regimen (N=40)	P value
Response			
Yes n (%)	34 (85.0%)	21 (52.5%)	0.002
No n (%)	6 (15.0%)	19 (47.5%)	

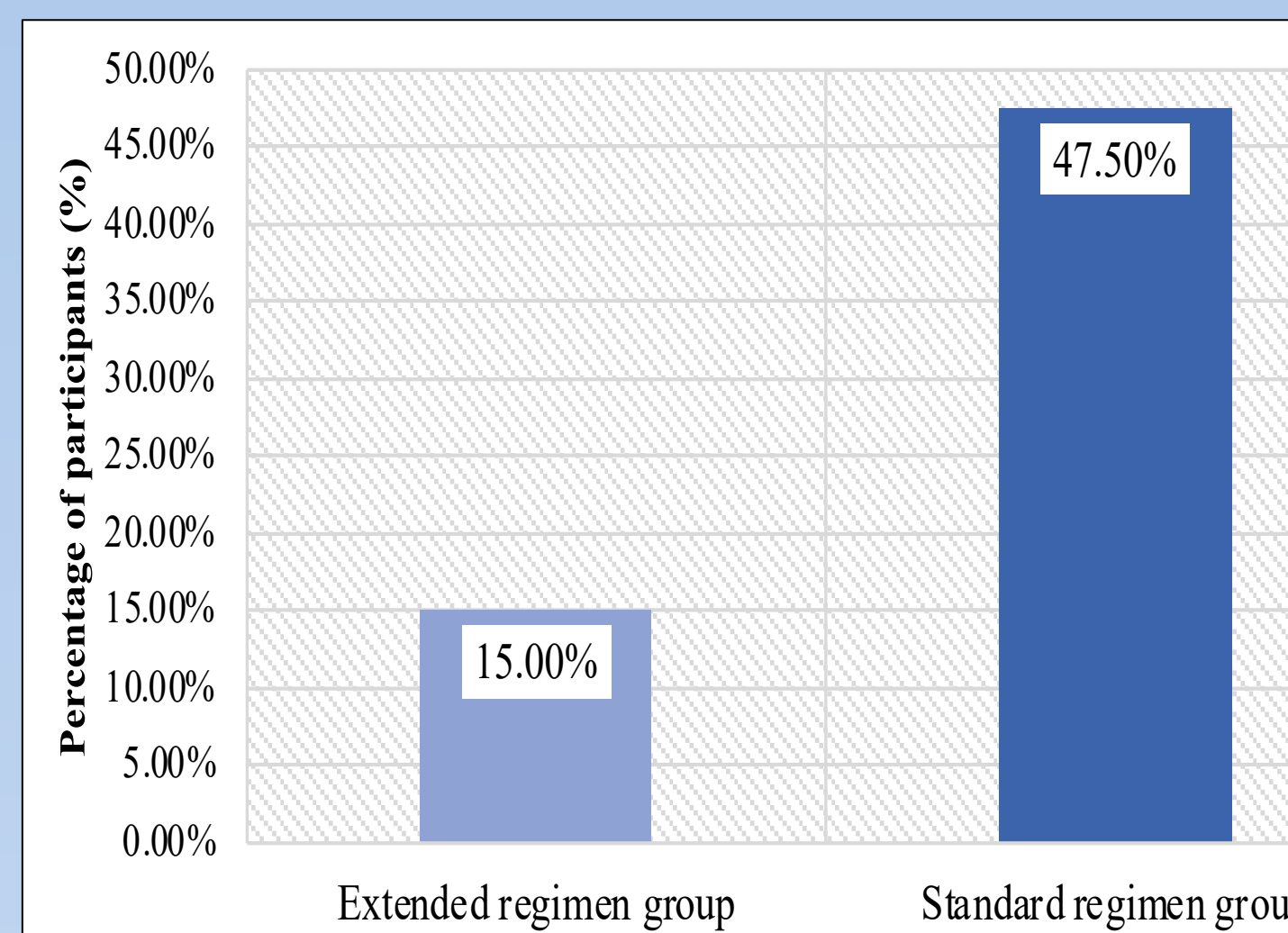
Extended Regimen



Standard Regimen



Need for 5 mg dose



Pregnancy Outcomes

Parameter n (%)	Extended Regimen (N=40)	Standard Regimen (N=40)	P-value
Clinical pregnancy rate per patient	14/40 (35.0%)	13/40 (32.5%)	0.813
Pregnancy rate per cycle	14/62 (22.58%)	13/85 (15.29%)	0.286
Multiple pregnancy	1/14 (7.1%)	0/13 (0.0%)	1.000
Abortion rate	5/14 (35.7%)	3/13 (23.1%)	0.678

- None required Injection Gonadotropin in extended regimen (0% vs. 15.8%, $p = 0.025$)**
- Multi-follicular development (15.0% (6/40) vs. 17.5% (7/40), $p = 0.762$) were comparable**
- No OHSS in either group**

Conclusion

The extended 10-day letrozole regimen significantly improved follicular response without increasing adverse outcomes like OHSS. It reduced the need for dose escalation or gonadotropin use and showed a trend toward higher per-cycle conception. These findings support the extended regimen as a safe and effective option for ovulation induction in women with PCOS.

References

- Misso ML, Wong JLA, Teede HJ, Hart R, Rombauts L, Melder AM, et al. Aromatase inhibitors for PCOS: a systematic review and meta-analysis. Hum Reprod Update. 2012;18(3):301–12.
- Zhu X, Fu Y. Extending letrozole treatment duration is effective in inducing ovulation in women with polycystic ovary syndrome and letrozole resistance. Fertil Steril. 2023;119(1):107–13.
- Mandelbaum RS, Agarwal R, Melville S, Violette CJ, Winer S, Shoupe D, et al. A comparison of letrozole regimens for ovulation induction in women with polycystic ovary syndrome. F&S Rep. 2024;5(2):170–5.